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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,234	10/22/2001	Maria Marino	214038US0PCT	2544

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,234	MARINO ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-7 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10 November 2004 has been entered in full. Claim 10 is amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 4-7 and 10 are under consideration in the instant application.

Claim Rejections - 35 USC § 112, first paragraph

1. Claims 4-7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth for claims 4-7 and 10 at pg 2-5 of the previous Office Action (12 July 2004).

The claims are directed to a peptide having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration. The claims recite a pharmaceutical composition comprising an effective does of a peptide compound having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration, and at least one pharmaceutically acceptable inert ingredient. The claims also recite a method of treating Multiple Sclerosis in a human being, comprising administering to a patient an effective amount of a peptide compound having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration.

Applicant's arguments (10 November 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that while it is true there are difficulties in extrapolating the results obtained from rodent models to an effective treatment of the disease of MS in human beings, the art (for example, Hart et al.) indicates that rodent models are of very important benefit in providing an indicator of the possible effectiveness of a given proposed therapeutic regimen. Applicant argues that in the present specification, Example 1 describes an assay test involving the claimed peptide of formula I in which the peptide was tested in four groups of SJL female mice at the age of 6-15 weeks. Applicant contends that while this model and results obtained may not be a completely reliable indicator of the effect the peptide may have when administered to human beings suffering from MS, nevertheless, the model employed and result obtained are sufficiently suggestive of a possible therapeutic use in the treatment of human beings. Applicant also cites MPEP § 2107.03 (I)(III) to emphasize that the text of the specification has provided a reasonable correlation between the stated therapeutic utility of a method of treating a subject suffering from MS and the data of the assay conducted with the peptide of formula I.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the specification teaches that two groups of mice are immunized intraperitoneally with the peptide compound of formula I or II (pg 11, lines 1-5). The specification further discloses that after 2 weeks, experimental allergic encephalitis (EAE) is induced all groups (including control) by challenge with P81-100 and mice are observed daily for clinical signs of EAE (pg 11, lines 8-22). Finally, the specification teaches that mice treated with the peptide of SEQ ID NO: 1 (formula 1) did not develop EAE (pg 12, lines 7-12; Table 1). The specification

concludes that "Assay 1 shows that peptide compound[s] of the present invention are able to delay the onset of clinical signs of the disease, diminishing the severity and increasing the survival rate of treated mice" (pg 7, lines 28-30). However, Assay 1 of the specification administers the claimed peptide of Formula I *before* inducing EAE (pg 11, lines 1-11). Since EAE is induced in mice by challenge with MBP fragment P81-100, isn't it possible that the claimed peptide of SEQ ID NO: 1 (compound I), which is a variant of P81-100, simply blocks the inducement of EAE since it is administered before the challenge? This mechanism would be a functional inactivation of T cells, rendering them incapable of eliciting an immune response to the P81-100 fragment. For example, relevant literature teaches that EAE in guinea pigs and rats can be suppressed if the animals are treated with MBP in IFA before or after immunization with MBP+CFA (Swanborg, R.H., Immunol Rev 184: 129-135, 2001; pg 131, 2nd full paragraph through the 4th full paragraph). Furthermore, the instant specification does not teach any methods or working examples indicating the induction of EAE in mice *and then the administration of the claimed peptide compound of formula I.* The specification does not teach the manifestation of MS (or EAE in the mouse) and the subsequent administration of the claimed peptide compound of Formula I. The state of the art is such that multiple sclerosis is a human autoimmune disease without fully effective treatment and largely unknown pathogenesis (including genetic factors) (Lutton et al., Exp Biol Med 229:12-20, 2004; pg 12, 1st paragraph; Pender et al., Intern Med J 32(11): 554-563, 2002; pg 555, col 1). t' Hart et al. also disclose that the cause of the neurological deficit in MS and EAE is still poorly understood and it is clear from animal models that CNS inflammation and demyelination do not fully account for the irreversible neurological deficit in advanced MS (Curr Opin Neurol 16 : 375-383, 2003; pg 379.

1st full ¶). Lutton et al. states that "several therapeutic agents for the treatment of MS have been tested and studied, but the management of the disease still remains complex and unreliable" (pg 16, last ¶ in col 2). Therefore, a large quantity of experimentation would be required by the skilled artisan to treat multiple sclerosis in humans with the claimed peptide compound of Formula I.

Additionally, although MPEP § 2107.03 relates to utility requirements of an application, Applicant has not established that the data generated from Assay 1 of the specification is correlated to treating multiple sclerosis. For instance, the mice utilized in Assay 1 are administered the claimed peptide compound of Formula I *before* the induction of EAE. This example does not correlate with the claimed method of treating multiple sclerosis because the mice do not manifest EAE before the administration of the compound. The claimed invention would correlate to a working example wherein the mice manifested EAE and then were administered the claimed peptide compound of Formula I. Therefore, undue experimentation would be required of the skilled artisan to treat a patient suffering from Multiple Sclerosis (MS) by administering to the patient the peptide compound of formula I (SEQ ID NO: 1). A large quantity of experimentation would be required by one skilled in the art to determine the optimal dosage, duration, and route of administration of the peptide of SEQ ID NO: 1 for treatment of MS. The experiment in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and

physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily treat MS by administering the peptide of SEQ ID NO: 1.

Applicant is encouraged to submit any pre- or post-filing date references or evidence in the form of a declaration under 37 C.F.R. 1.132 to support the claimed invention.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine the optimal dosage, duration, and route of administration of the peptide and to treat multiple sclerosis in humans by administration of the peptide of SEQ ID NO: 1, the lack of direction/guidance presented in the specification regarding the same, the complex nature of the invention, the state of the prior art indicating the differences in EAE and MS (see 't Hart et al., Lutton et al., Pender et al., and Swanborg), and the unpredictability of the effects of the claimed peptide in a human for the treatment of multiple sclerosis (see discussion and recited references), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
11 January 2005

ELIZABETH KEMMERER
PRIMARY EXAMINER